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Spherical and tubule nanocarriers for sustained drug release

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We discuss new trends in Layer-by-Layer (LbL) encapsulation of spherical and tubular cores of 50–150 nm diameter and loaded with drugs. This core size decrease (from few micrometers to a hundred of nanometers) for LbL encapsulation required development of sonication assistant non-washing technique and shell PEGylation to reach high colloidal stability of drug nanocarriers at 2–3 mg/mL concentration in isotonic buffers and serum. For 120–170 nm spherical LbL nanocapsules of low soluble anticancer drugs, polyelectrolyte shell thickness controls drug dissolution. As for nanotube carriers, we concentrated on natural halloysite clay nanotubes as cores for LbL encapsulation that allows high drug loading and sustains its release over tens and hundreds hours. Further drug release prolongation was reached with formation of the tube-end stoppers.

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Polyelectrolyte coated drug nanocarriers

Spherical nanocarriers, especially emulsion and polymer based systems, due to low toxicity of used materials and easiness of preparation are under intensive investigation for encasing therapeutic compounds. A wide range of drugs and reporting molecules have been incorporated into the nanovehicles that release the drugs in a prolonged or stimuli-responsive manner. Several nanocrystalline drug formulations have also been approved for medical usage or are in clinical trials [1,2].

A state of art in the field is Layer-by-Layer (LbL) coated nanocarriers since this approach allows for combining drug-loaded core matrix with a shell of variable architecture that can consist of polyelectrolytes, proteins, nanoparticles, and selected molecules of low molecular weight. On the basis of electrostatic interaction between adsorbing layers, LbL shell preparation does not require harsh conditions to interlock different components together in the same coating. As an advantage, its architecture in the direction normal to the core surface is decided beforehand [3–5]. The possibility of scaling-down and combining with different core preparation techniques makes LbL assembly a highly promising approach for nanomedicine applications.

Nevertheless, only within the recent five years the design of the LbL nanovehicle systems reaches the level of properties desirable for efficient systemic delivery: minimum toxicity due to biodegradable materials, stability of nanocolloid as an isotonic formulation, prolonged release of encased drug *in vitro* and *in vivo*, effective endosomal escape, and extended serum half-life that allows for prolonged exposure of cells to the treatment, active targeting and tumour cell uptake [1,6]. In a proof-of-concept study, Hammond *et al.* [7•] recently demonstrated a systemic co-delivery of doxorubicin and siRNA in NCr nude mice bearing subcutaneous xenograft tumours of luciferase-expressing MDA-MB-468 cells via 120 nm LbL coated liposomes. Liposomes containing 5.5 wt.% of doxorubicin were used as a core. By assembling MRP1 siRNA in alternation with poly-L-arginine as a multilayer shell, a high loading of the gene silencing RNA per nanoparticle was reached. A layer of hyaluronic acid deposited atop the shell efficiently shields it from recognition by immune system and enhances the nanocapsules uptake by tumour tissue through the interaction of hyaluronic acid with CD4 glycoprotein. In another study, LbL-coated paclitaxel (PTX) nanoparticles with attached tumor-specific mAb 2C5 antibody effectively target the nucleosome monolayer in the ELISA assay. Attached antibody enhances *in vitro* toxicity of the nanocapsules towards MCF-7 and BT-20 cancer cell lines [8]. Yet in another work, bovine serum albumin (BSA) nanoparticles of a 200 nm diameter modified with polyallylamine hydrochloride/polystyrene sulfonate (PAH/PSS) multilayers were used for encapsulation of doxorubicin and covalent modification with aptamer AS1411 to target the over-expressed nucleolin on cancer cell membrane [9].

Apart from preset architecture of the coating as above, the polyelectrolyte shell stabilizes nanocrystals of poorly